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10/005,131	12/05/2001	Geoffrey Goldspink	10103-004	8321

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,131	GOLDSPINK, GEOFFREY	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-35,40-42,51,58-62,67-69,78,97 and 98* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-35,40-42,51,58-62,67-69,78,97 and 98* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Action of June 30, 2005 on December 29, 2005. Claims 1-30, 36-39, 43-50, 52-57, 63-66, 70-77, 79-96 are cancelled. Claims 31, 41, 42, 51, 58, 68, 69, 78 are amended. Claims 97 and 98 are new.

Claims 31-35, 40-42, 51, 58-62, 67-69, 78, 97, 98 are under consideration.

As a reminder, as indicated in the Office Action of June 30, 2005, that as a result of the restriction requirement filed February 18, 2004, the scope of analysis for the instant invention is limited to a method of treatment of an animal comprising administering a plasmid vector comprising a myosin light chain enhancer and a viral promoter operatively liked to a sequence that generates a polynucleotide sequence encoding a polypeptide of therapeutic use. Claims which contain embodiment beyond this scope were not considered as part of the analysis.

Withdrawn Rejections

35 U.S.C. § 103(a)

Applicant's arguments, see page 10-11, filed June 30, 2005, with respect to the rejection of claims 58-62, 67-69, 78 have been fully considered and are persuasive. Applicant has indicated that Fenjves focuses on systemic distribution of apolipoprotein E secreted by grafts of epidermal keratinocytes and that nothing in Fenjves suggests or motivates a skilled artisan to modify the teachings of Goldspink by inserting the cDNA sequence of apoE into the expression plasmid taught by Goldspink. The rejection of claims 58-62, 67-69, 78 has been withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31-35, 40-42, 51, 58-62, 67-69, 78 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. It is noted that new claims 97 and 98 do not overcome any of the rejections set forth in the enablement rejection of June 30, 2005 and are thus newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record discussed on June 30, 2005.

Response to Arguments

Applicant's arguments filed December 29, 2005 have been fully considered but they are not persuasive.

It is noted that Applicant has amended claims 31 and 58 to a narrower scope of, "a method for treatment of a metabolic disorder or condition related to an alpha-galactosidase A deficiency (Applicant's response, pages 4-5)," and have addressed the issue regarding the broad scope that the claimed invention was readable on the

treatment of any disease (Office Action, June 30, 2005, pages 9-12). While Applicant has narrowed the scope of the claimed invention, the amendments and arguments provided by Applicant to overcome the Examiner's rejections are not persuasive, as follows.

Applicant indicates that it is well-known in the art that elevated levels of alpha-galactosidase a have positive effect in patients with Fabry disease (Applicant's response, page 5, 7th parag.). Applicant indicates that Mignani and Cagnoli, 2004, J. of Nephrology, 17: 354-363 teach that enzyme replacement therapy resulted in reduction in storage of the glycophingolipids's substrate from several organs and tissues and consequently, improved signs and symptoms of Fabry's disease; that Bongiorno et al., 2003, J. Eur. Acad. Dermatol. Vernerol., 17: 676-679 teach that increase in mean creatinine clearance, significant improvement in the acroparaesthesias and in hypohidrosis after 12 months of therapy were indicators of treatment; and Wilcox, et al., 2004, Am. J. Hum. Genet., 75: 65-74 teach that continuous decrease in plasma GL-3 levels sustained endothelial GL-3 clearance, stable kidney function, and a favorable safety profile. Applicant provides these post-filing arts to indicate that the claimed invention was enabled at the time of invention. However, the Examiner does not find that these arts indicate that the claimed invention was enabled at the time of invention. The art teaches that alpha-Gal A protein was administered to mouse models of Fabry's disease and to human patients (Mignani and Cagnoli, page 2, under "Early preclinical studies" and "Clinical trials"; Bongiorno et al., page 677, Materials and Methods, 2nd parag.; Wilcox, et al., page 65, 1st col., 2nd parag. to 2nd col., 1st parag.). However, the

arts do not teach that nucleic acids were administered to patients or mouse models of Fabry disease. Applicant is reminded that an the art teaches that the artisan cannot predict that the expression levels of alpha-Gal A driven by an expression vector are at levels that a therapeutic effect can be seen (Office Action, June 30 2005, pages 6-8). As such, the art does not provide support that the claimed invention was enabled at the time of the invention.

Regarding the issue that the interpretation of the results obtained in mice is inadequate when applied to humans, Applicant indicates that the fact cannot be ignored that any candidate for a drug is initially tested in animals and that mice are primary targets for testing, and as such, numerous lines of mice with different deficiencies have been created to serve as models for various diseases. Applicant also indicates that Ohshima et al. characterized a mouse model of Fabry disease, wherein the mouse exhibited symptoms similar to that of the human disease (Applicant's response, page 6, 4th parag. to page 7). In response, the Examiner was not questioning whether the mouse described in the specification was a model of a human disease. Rather, the issue at hand was that an artisan cannot readily extrapolate that studies carried out in mice are readily applied to humans. As indicated by the Office Action, June 30, 2005, page 8, the art teaches that there is unpredictability in gene transfer studies that experimental animals have not been borne out in human safety and efficacy trails. As this applies to the instant invention, even if the Applicant were to show that the levels of expression driven by transgene construct in the mice described in the specification were at levels that had beneficial effects in mice, an artisan cannot readily extrapolate that

the vector would necessarily express at levels similar to mice or that the levels expressed by the vector in mice would necessarily be at levels that are beneficial to humans or to any other animal that needs treatment. As the art teaches this unpredictability, an artisan cannot use the claimed invention without further guidance.

For these reasons, the Applicant's response does not overcome the Examiner's rejections and thus, the claims remain rejected.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31-35, 40-42, 51, 58-62, 67-69, 78 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 41, 42, 68, 69 remain rejected as they are indefinite in their recitation of the phrase "comprising...genomic sequences flanking said expression cassette" since the expression cassette implicitly comprises genomic sequences. Also, claims 31 and 58 (and their dependent claims) remain rejected as the method steps do not recite any step relating to "treatment".

Response to Arguments

Applicant's arguments filed December 29, 2005 have been fully considered but they are not persuasive. While Applicant has amended claims 41, 42, 68, 69 to remove the word, "further," the sequences flanking the expression cassettes (i.e. the promoter

and the 3' end of the nucleic acid encoding the gene of interest) are genomic sequences that it is not clear how the claim further limits the base claim. Regarding the rejection that there is no recited step relating to "treatment," in claims 31 and 58, Applicant has not addressed this issue. Thus, the claims remain rejected.

It is noted that Applicant has addressed the issue of the method steps not reciting an object to which the administration steps is directed to, as indicated in the Office Action, June 30, 2005, page 13, as Applicant has amended the claim. This aspect of the rejection, as it applies to claims 31 and 58 is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-35,40-42, 51 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Goldspink et al (WO/94/28151) in view of Jeang et al., 1984, Molecular and Cellular Biology, 4: 2214-2223, for reasons of record discussed June 30, 2005.

Response to Arguments

Applicant's arguments filed December 29, 2005 have been fully considered but they are not persuasive.

Applicant indicates that the teachings of Jeang et al. do not remedy the deficiency of Goldspink (Applicant's response, page 9, 3rd parag.) as Jeang et al. discloses the expression of a specific viral protein in nonpermissive rodent cells after cytomegalovirus (CMV) strain infection. While Applicant provides this argument, the Examiner does not find it persuasive because the Examiner was not focusing on the CMV protein that Jeang et al. were characterizing, but was focused on the characteristics of a CMV promoter (Office Action, June 30, 2005, page 15). Jeang et al. teach that the physical characteristics of the CMV promoter and also indicate that these characteristics are what contribute to strong, constitutive expression in mammalian cells (see Jeang et al., page 2221, 2nd col. to page 2222, 1st col.). Thus, it would have been obvious for an artisan to replace the beta-cardiac myosin heavy chain promoter used in Goldspink with the CMV promoter described by Jeang, et al., in order to obtain an expression vector that drove expression of a transgene at high levels.

Thus, the rejection of claims 31-35, 40-42, 51 remains.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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JH

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER